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ANTONELLI, TERRY, STOUT & KRAUS, LLP
1300 NORTH SEVENTEENTH STREET
SUITE 1800
ARLINGTON, VA 22209-3873

EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,455	RAOULT, DIDIER M	
	Examiner	Art Unit	
	JaNa Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. The amendment filed March 30, 2009 has been entered. Claims 1-14 have been cancelled. Claims 15-25 have been newly added. Claims 15-25 are under consideration in this office action.

Priority

2. Receipt is acknowledged of a certified copy of the FR 02/08324 application referred to in the oath or declaration or in an application data sheet. However, should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d) prior to declaration of an interference, a translation of the foreign application should be submitted under 37 CFR 1.55 in reply to this action. Further, to obtain priority Applicant needs to submit an amendment to correct the first line of the specification. Applicant should have included in the amendment of the instant specification the following: This application is a 371 of PCT/FR03/02050 filed 02/07/03, which claims foreign priority to FR 02/08324 filed 3/07/02.

Withdrawal of Rejections

3. The following rejections have been withdrawn in view of applicants' amendments:

a) The rejection of claims 1-14 under 35 U.S.C. 112, second paragraph;

b) The rejection of claims 1-9 and 12-14 under 35 U.S.C. 102(b) as being anticipated by Dorval et al; and

c) The rejection of claims 10-11 under 35 U.S.C. 103(a) as being unpatentable over Dorval et al., in view of La Scola et al.

Response to Arguments

4. Applicant's arguments with respect to claims 1-14 have been considered but are moot in view of the new ground(s) of rejection.

New Grounds of Rejection Necessitated By Amendments

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 20, 22 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claims 20 and 22, recite alternative limitations which are improperly expressed. Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. One acceptable form of alternative expression, which is commonly referred to as a Markush group recites members as being "selected from the group consisting of A, B and C". Another acceptable form recites "selected from 1, 2, 3, or 4." Applicant may correct this by amending the claim to recite the appropriate language.

b) Claim 24 is rejected because acronyms and/or abbreviations like H.I.V and C.M.V. must be spelled out when used for the first time in a chain of claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 15-21 and 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dorval et al., (US Patent 5,561,045) in view of Hanke (DE 100 00 322A1, see the machine translation document from the EPO, pages 1-11).

Claim 15 is drawn to an in vitro serological diagnosis method for detecting the presence of antibodies specific to an infectious microbial agent in a sample to be tested, which comprises: a) depositing on a solid substrate a first antigen Ag_1 comprising a whole *Staphylococcus aureus* bacterium which comprises protein A and at least one second antigen Ag_2, wherein said second antigen Ag_2 is an infectious microbial agent, and b) contacting said first antigen Ag_1 and said at least one second antigen Ag_2 with a sample to be tested causing said first antigen Ag_1 and said at least one second Ag_2 to react with a sample to be tested, and c) detecting whether a human immunoglobulin Ac_1 in said human serum reacts with said first antigen Ag_1 by causing the reaction product Ag_1- Ac_1 to react with a detection substance, wherein said detection substance reacts with said human immunoglobulin and not with said first antigen (Ag_1), and wherein the reaction product Ag_1-Ac_1 is formed from the reaction of said human immunoglobulin Ac_1 and said first antigen Ag_1, and d) providing a controlled

sample containing a human serum to be tested for detecting whether said human immunoglobulin react with said first antigen.

Claim 16 is drawn to the detection substance being a secondary detection antibody Ac_1 which is a labeled anti-human immunoglobulin which does not react with protein A. Claim 17 is drawn to the anti-human immunoglobulin being goat immunoglobulin or chick immunoglobulin. Claim 18 is drawn to the detection substance being labeled by fluorescent marking. Claim 19 is drawn to the method further comprising: performing a series of tests at increasing dilutions of the sample to be tested with the detection substance Ac_1, wherein the detection substance Ac_2 is an immunoglobulin conjugated with a fluorescent substance, and verifying whether a reaction product Ag_1-Ac_1-Ac_2 can be detected by fluorescence at a dilution of the sample to be tested of 1/200 or less, wherein the reaction product Ag_1-Ac_1-Ac_2 is formed by the reaction of the human immunoglobulin Ac_1, the first antigen Ag_1, and the detection substance Ac_2. Claim 20 is drawn to the infectious microbial agent of Ag_2 being selected from a bacterium, a virus, a parasite or a fungus. Claim 21 is drawn to the second antigen being an intracellular bacterium or a virus. Claim 24 is drawn to Ag_2 is H.I.V.

Claim 25 is drawn to a diagnosis kit for detecting the presence of antibodies specific to an infectious microbial agent in a sample to be tested, which comprises: a solid substrate comprising a second antigen Ag_2 which is an infectious microbial agent, one positive controlling inclusion comprising a human serum in the sample to be tested which comprises a first antigen Ag_1 containing a whole *Staphylococcus aureus*

bacterium containing protein A, and at least one reagent which can detect the presence of a reaction product of said first antigen with a human immunoglobulin Ac_1 comprising a detection substance Ac_2 which comprises a labeled immunoglobulin which is an anti-human immunoglobulin which does not react with protein A.

Dorval et al., teach processes that permit the ability to detect simultaneously a variety of classes of immunoglobulin specific for the same analyte (col.2, lines 30-34). Dorval et al., teach the enhancement of sensitivity using specific binding proteins like Protein A within immunoassays (col. 2, lines 35-40). Dorval et al., teach anti-IgA-IgG and anti-IgM-IgG and protein A (col. 3, lines 19-20). Dorval et al., teach a solid support with a first antigen containing Protein A, a second microbial antigen, the addition of the detection agent which is labeled anti-human immunoglobulin with does not react with Protein A, see Figures 1a-1f. Dorval et al., teach a variety of kits with include the detection reagents, the binding protein A, and immunoglobulins (col. 4, lines 40-49). Dorval et al., teach labels to be chromophores, fluorophores, metal sols, enzyme labels and colorimetric particles (col. 6, lines 48-68). It is noted, that fluorescein is a common type of fluorophore. Dorval et al., teach the sensitivity of a wide variety of assays is enhanced with the use of the immunoglobulin and Protein A, including direct, indirect, competitive and sandwich type heterogeneous and homogenous assays (col. 9, lines 16-25). Dorval et al., teach the reagents may be advantageously in virtually any type of immunoassay where it is desirable to prevent the interaction of Protein A with a portion of an immunoglobulin; thus allowing the antigen to be bound to a solid phase and the

presence of different classes of specific antibodies to be determined (col. 9, lines 25-33). Dorval et al., teach the detection of HIV virus (col. 9, lines 37-42).

Hanke teaches strips for western blotting which include on a carrier, (i) a serum control zone which will produce a band flowing incubation with patient serum and (ii) at least one conjugate control zone which will produce a band following incubation with a labeled anti-patient immunoglobulin antibody from a different animal species (abstract). Hanke teaches multiple control zones which make for improved differentiated, additional control possible and provides improved interpretation of test results (page 1 of the translation). Hanke teaches a labeled conjugated animal antibody which is specific for human immunoglobulin (page 2).

Therefore, it would have been prima facie obvious at the time of applicants invention to modify the *in vitro* serological diagnosis method in which, in a sample to be tested, the presence is detected of antibodies specific to an infectious microbial agent, as taught by Dorval et al., wherein the modification incorporates the use a control zone as taught by Hanke in order to provide a method that establishes detection of human immunoglobulin interaction. Furthermore, there is a reasonable expectation of success in incorporating the methods of Dorval et al., and Hanke since both teach providing a sample to be tested is react with solid-substrate having a deposited first and second antigen and detecting whether the human immunoglobulin reacts with the antigen, especially when no change in their respective functions, thus the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Furthermore, one of ordinary skill in the art at the time the invention was

made would have been motivated to extend the methods taught by Dorval et al., and Hanke while incorporating the additional bacterial and viral pathogens into the *in vitro* serological diagnosis as in order to arrive at the claimed invention with provide assays containing serum and conjugate control zones when detecting infectious microbial antigens.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dorval et al., (US Patent 5,561,045) and Hanke (DE 100 00322) in view of La Scola et al (Journal of Clinical Microbiology, 1996; 34(9): 2270-2274).

Claim 22 is drawn to the second antigen being Chosen from among bacteria of the genus *Rickettsia, Coxiella, Bartonella, Tropheryma, Ehrlichia*, *Chlamydia*, *Mycoplasma, Treponema, Borrelia,* and *Leptospira.* Claim 23 is drawn to the second antigen corresponding to the infectious microbial agent is a bacterium responsible for endocarditis.

Dorval et al., and Hanke have been discussed above, however neither teach the second antigen being *Bartonella* or a bacterium being responsible for endocarditis.

La Scola et al, teach serological cross-Reactions *between Bartonella Quintana, Bartonella henselae,* and *Coxiella burnetti. Bartonella Quintana,* is known to be associated with endocarditis, while *Bartonella henselae* is known to be associated diseases in AIDS patients (page 2270).La Scola et al., teach a method of performing serological diagnostic test for *Bartonella* and *C. burnetti* infections (page 2270). The prior art discloses immunoglobulin G (IgG) anti-phase I titer of equal to or greater than 1:800 and an IgA anti-phase II titer were considered diagnostic for infection. La Scola et al teach that human patients with titers of equal to or greater that 1:1,600 or antibody against *B. henselae* or *B. Quintana* antigens were also considered diagnostic for infection (page 2272). La Scola et al., teach positives being found (IgG, 1:100) (IgG 1:200) (page 2271). The method of La Scola et al comprises the following steps: a) Serum samples were taken from patients; b) Bacterial antigen being deposited on 30 well microscope slides, and sera was serially diluted and applied to the wells; c) Slides were incubated in a moist chamber for 30 minutes, washed, dried and overlaid with labeled goat anti-human IgG antibodies; d) Interaction of antigen and antibody was observed (page 2271). La Scola et al., teach Western blotting was used to determine the interaction of antigen and antibody (page 2271).

Therefore, it would have been prima facie obvious at the time of applicants invention to modify the *in vitro* serological diagnosis method in which, in a sample to be tested, the presence is detected of antibodies specific to an infectious microbial agent, as taught by Dorval et al., and Hanke wherein the modification incorporates the use of variety of microbial agents as taught by La Scola et al., in order to provide detection of a

wide variety of agents. Furthermore, there is a reasonable expectation of success in incorporating the methods of Dorval et al., and Hanke in view of La Scola et al., since both teach providing a sample to be tested is react with solid-substrate having a deposited first and second antigen and detecting whether the human immunoglobulin reacts with the first antigen, especially when the steps and components of the method have been combined with no change in their respective functions, thus the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to extend the methods taught by Dorval et al., and Hanke while incorporating the additional yet equivalent microbial antigens associated with AIDS and HIV into the *in vitro* serological diagnosis as taught by Dorval and Hanke in order to arrive at the claimed invention with provide enhanced sensitivity using specific binding proteins like Protein A within immunoassays.

Conclusion

8. No claims allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached Monday thru Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Robert Mondesi, can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/JaNa Hines/
Examiner, Art Unit 1645

/Mark Navarro/

Primary Examiner, Art Unit 1645